

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

REC'D 3 1 OCT 2005

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Applicant's or agent's file reference
P792PC00

FOR FURTHER ACTION

See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)

International application No.
PCT/DK2004/000454

International filing date (day/month/year)
25.06.2004

Priority date (day/month/year)
26.06.2003

International Patent Classification (IPC) or both national classification and IPC
C07K1/04, C07B61/00

Applicant
CARLSBERG AS

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the opinion
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand

25.04.2005

Date of completion of this report

02.11.2005

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/DK2004/000454

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-70 as originally filed

Claims, Pages

1-143 as originally filed

Drawings, Sheets

1/14-14/14 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

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5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	
	No: Claims	1-143
Inventive step (IS)	Yes: Claims	
	No: Claims	1-143
Industrial applicability (IA)	Yes: Claims	1-143
	No: Claims	

2. Citations and explanations

see separate sheet

Re Item V

**Reasoned statement with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement**

Reference is made to the following documents:

- D1: J. Comb. Chem. 3, 2001, pages 45-63;
- D2: J. Comb. Chem. 3, 2001, pages 34-44;
- D3: Chemistry - A European Journal 5(4), 1999, pages 1218-1225;
- D4: Tetrahedron Lett. 44(19), 5 May 2003, pages 3835-3838.

1) D1 (see i. a. Figure 2) discloses the formation of peptide libraries ending with a polycyclic derivative prepared with the use of the Pictet-Spengler reaction, whose intermediate is known to be an N-acylimminium ion. To this respect see also Scheme 8 of the same document. In particular, scheme 8 of the present document shows an intramolecular Pictet-Spengler reaction which takes places starting from a compound falling into the wording of claims 1 ff.

D2 discloses (see Scheme 5) the preparation of peptide isosters ending in a polycyclic derivative by the use of the Pictet-Spengler reaction. These isosters can immediately be used as building blocks in the preparation of libraries, and this is evident already in the title. The use of Pictet-Spengler in this reaction is, however, intermolecular.

D3 discloses the preparation of polycyclic compounds from N-terminal peptide aldehydes immobilized on a support. Though the use of those in the preparation of libraries is not alluded to in the title, it is sufficient to read the first lines of the introduction and the possibility of their use as building blocks in the preparation of libraries becomes evident to the skilled artisan. Figure 1 shows that the Pictet-Spengler reaction leading to cycles can also be intramolecular.

D4 discloses the use of the Pictet-Spengler reaction in the preparation of peptide libraries ending with polycyclic compounds. The examples provided in this disclosure refer only to intermolecular Pictet-Spengler reactions.

On the basis of the above disclosures it is concluded that claims 1-143 of the present application are deemed to lack novelty under Art. 33(2) PCT on the basis of D1 and D3. The applicant is however reminded that the structure of claim 1 ff. is also anticipated in the disclosures D2 and D4, since the definition of "nucleophile" is too generic to permit an

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assessment of what is really meant (probably the use of the N-heterocyclic atom of a tryptophane residue as nucleophile).

2) On the basis of D1-D4, the objective problem underlying the present application consists in the provision of alternative libraries and method to prepare them. There is no appreciable difference between the present application and the documents cited above. No unsuggested technical feature is evidenced, nor is any surprising effect brought to the attention of the skilled person. Therefore an inventive step under Art. 33(3) PCT cannot be recognized for claims 1-143 of the present application.

3) Claims 1-143 are endowed with industrial applicability under Art. 33(4) PCT.